

## **REMARKS**

Claims 39-44 are currently pending.

### ***Priority Claim***

The Examiner acknowledges that applicants have claimed priority to U.S. Provisional Patent Application No. 60/062,816 filed on October 24, 1997. The Examiner has denied the priority claim under 35 U.S.C. 112, because the disclosure regarding PRO246 as a possible virus vector allegedly does not enable one skilled in the art to use the antibody without undue experimentation.

As will be apparent from the discussion below, Applicants submit that the disclosure does provide sufficient information to enable some one skilled in the art to practice the claimed invention. Accordingly the effective filing date of this application is October 24, 1997.

### ***Claims Rejections - 35 U.S.C. § 112, first paragraph***

Claims 39-44 were rejected under 35 U.S.C. §112, first paragraph, for alleged lack of enablement in the first Office Action dated October 2, 2002. Applicants filed a response February 19, 2003. The Examiner in this Office Action has indicated that this rejection is withdrawn on the basis that PRO246 protein has biological activity of inhibiting VEGF-stimulated epithelial cell growth.

Applicants rely on the ability of the PRO246 protein to function as viral receptors to claim priority to October 24, 1997. Accordingly, Applicants herewith provide reasons why this rejection is improper based on PRO246 proteins activity as a viral receptor.

35 U.S.C. §112, first paragraph, requires that an invention be described in such full, clear, concise and exact terms as to enable a person skilled in the art to make and use the same. The specification need not explicitly teach those in the art to make and use the invention; the requirement is satisfied if, given what they already know, the specification teaches those in the art enough that they can make and use the invention without "undue experimentation" Amgen Inc. v. Hoechst Roussel, Inc. 65 USPQ 2d

1385-1421, 1400 (Fed Cir 2003) citing Genentech, Inc. v. Novo Nordisk, A/S 42 USPQ 2d 1001, 1004 (Fed Cir. 1997). "That some experimentation is necessary does not constitute a lack of enablement" Amgen Inc. v. Chugai Pharmaceutical Co. Ltd. 18 USPQ 2d 1016, 1026.

The present application, and its earliest priority application 60/062,826 filed on October 24, 1997, provide the nucleic acid and amino acid sequence of the PRO246 polypeptide and indicate that this amino acid sequence shares significant homology to the human Cocksackie-adenovirus receptor. The disclosure further states that a portion of the PRO246 polypeptide has a significant homology with the human cell surface protein HCAR. Considering its significant homology to the human Cocksackie adenovirus receptor, Applicants further suggest the PRO246 polypeptide to be a novel cell surface virus receptor. The specification, at, for example, pages 118-199 and Examples 53-55, provides methods of transforming prokaryotic and eukaryotic cells with the PRO genes and methods of expressing the PRO gene in prokaryotic or eukaryotic cells. The specification at, for example, pages 139-144 and Example 57 describe methods of preparing antibodies to the PRO protein.

It was known in the art at the earliest priority date of the present application that HCAR is a human cellular receptor for the group B Cocksackie-viruses (CVB), and human subgroup C adenoviruses (Ad2 and Ad5) (see Tomko *et al.*, *Proc. Natl. Acad. Sci. USA* 94:3352-3356 (April 1997), a copy of which was previously submitted). In addition, virus assays were well known in the art at the earliest priority date of the present application, as demonstrated, for example, by the disclosure of Tomko *et al.*, *supra*. Such assays could be routinely used at the earliest priority date of the present application to identify the specific viruses that use the PRO246 polypeptide as their receptor. Consequently, based on general knowledge in the art and the disclosure of the present application, at the earliest priority date of the present application one was able to make and use the claimed invention, without undue experimentation.

The Examiner states that the assertion that the PRO246 polypeptide is a virus receptor is unreasonable given the allegedly large degree of divergence between

Applicants' protein and the most similar known virus. Accordingly, one skilled in the art would not be able to use the PRO246 polypeptide as a receptor for routine virological purposes.

In support of this argument, the Examiner states that alignment of Applicants' sequence with the human and mouse HCAR proteins indicates an overall similarity of 17% and a best local similarity of 27%. The Examiner cites McNicholl et al. as evidence that a protein with 100% homology to a portion of a virus receptor does not function as a virus receptor and Struyf et al. that alteration of even a few amino acids degrades the ability of another receptor to interact with virus.

First, Applicants note that both McNicholl et al. and Struyf et al. teach and disclose experiments altering a naturally occurring receptor. They are not comparing two different receptors. If certain alterations are made to a protein it can be rendered inactive. Such papers are not probative of whether a viral receptor must be highly homologous to the CAR receptor in order to be functional.

Second, the Examiner disputes that assays such as those of Tomko et al could be used to identify the specific viruses that use the polypeptide as a receptor and therefore alleges that the patent specification requires undue experimentation.

The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art. In re Wands 858 F.2d 731, 737.

Applicants note that Tomko et al. provides a general virus assay on page 3352. Tomko provides a method for transfecting NIH3T3 cells with a plasmid expressing the receptor. Tomko et al. provides a virus assay to be conducted with different viruses on the transformed cells. Clearly such assays could be routinely used at the earliest priority date of the present application to identify the specific viruses that use the PRO246 polypeptide as their receptor.

Finally, the Examiner argues that Applicants cannot rely on U.S. 5,942,606, as prima facie evidence that Applicants' specification is sufficient to teach those skilled in the art to make and use the claimed invention without undue experimentation.

Applicants cite U.S. Patent No. 5,942,606 as evidence that Applicant's specification does not require undue experimentation having due regard for the nature of the invention and the state of the art. The Examiner clearly declares that U.S. Patent No. 5,942,606 is fully enabled because the Examiner is citing U.S. Patent No. 5,942,606 against the Applicant as 102(e2) prior art. "To serve as an anticipating reference, the reference must enable that which it is asserted to anticipate. "A claimed invention cannot be anticipated by a prior art reference if the allegedly anticipatory disclosure cited as prior art is not enabled"" See Elan Pharmaceuticals, Inc. and Athena Neurosciences, Inc. v. Mayo Foundation for Medical Education and Research 2003 U.S. App Lexis 20195 (Fed. Cir. 2003) citing Amgen, Inc. v. Hoechst Marion Roussel, Inc. 314 F.3d 1313, 1354, 65 USPQ 2d 1385, 1416 (Fed. Cir. 2003). U.S. Patent No. 5,942,606 discloses a protein designated ACVRP, which is identical with the PRO246 polypeptide of the present application, and provides a very similar disclosure to the current specification. It simply provides sequence homology with HCAR as support for the sequence being useful as a viral receptor. The specification of the issued U.S. patent is devoid of any experimental data demonstrating the viral receptor activity of ACVRP, or identifying the specific viruses associated with this receptor. Accordingly, if U.S. 5,942,606 is fully enabled, Applicants currently claimed invention is similarly fully enabled. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

### ***Claim Rejections - 35 USC §102***

Claims 39-44 stand rejected under 35 USC § 102(e2) "as being anticipated by Lal et al. 5,942,606." Claims 39-44 were also previously rejected in the first Office Action, under 5 USC § 102(b) as being anticipated by Lal et al. The Examiner subsequently withdrew the 102(b) rejection on the basis that Applicants could claim priority to International Application PCT/US98/18824 filed Sept. 10, 1998 because that application disclosed the anti-VEGF biological activity of the PRO 246 protein.

As discussed above, the present application is entitled to the priority date of October 24, 1997, which precedes, by one month, the earliest priority date of Lal et al.

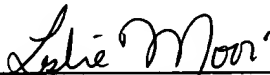
(November 24, 1997). Accordingly, Lal et al. is not prior art against the present application, and the present rejection under either 102 (b) or 102(e2) should be withdrawn.

In conclusion, the present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited. Should the Examiner find that there are any further issues outstanding, she is invited to contact the undersigned attorney at the telephone number shown below.

The Commissioner is authorized to charge any additional fees which may be required, including petition fees and extension of time fees, to Deposit Account No. 08-1641 (Attorney's Docket No. 39780-1618 P2C22).

Respectfully submitted,

Date: October 14, 2003

  
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